For these reasons, it is submitted that the present invention is patentable, and that all informalities in the claims have been corrected. Favorable reconsideration of the claims and allowance are respectfully requested.

Respectfully submitted,
CUSHMAN, DARBY & CUSHMAN

By _____
Lawrence A. Hymo
Reg. No. 19,057

1615 L Street N.W.
Washington, D.C. 20036

Telephone (202) 861-3000

UNITED STA / DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
07/551,644	07/12/90	HETTCHE	H 62748/87217P

EXAMINER
PICCONE, L

ART UNIT	PAPER NUMBER
152	14

DATE MAILED: 09/12/91

CUSHMAN, DARBY & CUSHMAN
ELEVENTH FLOOR
1615 L STREET, N.W.
WASHINGTON, DC 20036-5601

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 6/17/91 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), ___ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 1 - 18 are pending in the application.
   Of the above, claims _____ are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 1-18 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____, has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

15.

The examiner acknowledges receipt of the amendment filed June 19, 1991.

16.

Applicant's arguments with respect to claims 1-17 are have been considered but are deemed to be moot in view of the new grounds of rejection.

17.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

18.

Claims 1-12 and 18 are rejected under 35 U.S.C. § 103 as being unpatentable over Vogelsang U.S. 3,813,384 in view of art admitted in the specification.

Vogelsang teaches azelastine in a composition that can be

administered in drops, ointments or other "usual embodiments" that are used to administer azelastine (column 6, lines 65-70). Vogelsang teaches the administration of azelastine in amounts of from 0.4 to 4 mg (column 7, line 2). Also vogelsang shows the addition of numerous pharmaceutical. Adjuvants (column 43 lines 5-15). It would have been obvious to administer, the azelastine compositions of vogelsang directly to the nasal tissues or conjunctival sac to meet claims 1-4, 6-7, 9-12 because these are the areas to which medicament drops are normally applied. Claims 5, 8 and 18 would have been obvious because it is admitted in the specification that the claimed preseruahres are well known in the art and vogelsang discloses the use of adjuvant, in his compositions.

19.

Claims 13-17 are rejected under 35 U.S.C. § 103 as being unpatentable over Vogelsang U.S. 3,813,384 in view of art admitted in the specification as applied to claims 13-17 above, and further in view of in light of Barnes U.S. 158,564, Ashkenaz U.S. 2,995,308, Mendl U.S. 119,643 and Arp U.S. 2,457,024

Vogelsang discloses azelastine as an antihistamine. Vogelsand does not disclose the use of an eyedropper, a pump sprayer, an atomizer or a tube for dispensing ointment. Barnes discloses droppers for dispensing solutions. Applicant discloses the we of an eye dropper as a dispenser in claim 13.

Askenaz discloses a pump sprayer which may be used as applicant does in claim 14.

Mendl discloses an atomizer which functions in a manner similar to that disclosed on claims 15 and 16.

Arp discloses a tube for dispensing ointment as disclosed in column 17.

Claims 13-17 would have been obvious because they involve dispensing a known medication in a conventional manner.

No claim is allowed.

20.

Applicant's amendment necessitated the new grounds of rejection. Accordingly, THIS ACTION IS MADE FINAL. See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

21.

Any inquiry concerning this communication should be directed to Louis A. Piccone at telephone number (703)-308-4431.

Piccone/mh
September 10, 1991
9-6-91

BOX AF 3500 - 116 - 9152

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

15/Ext 2
Amd 7C
1/23/92

In re PATENT Application of

Helmut HETTCHE

Serial No. 07/551,664 Group Art Unit: 152

Filed: July 12, 1990 Examiner: L. Piccone

For: AZELASTINE-CONTAINING MEDICAMENTS

January 15, 1992

* * * * *

Hon. Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Dear Sir:

Responsive to the Office Action of September 12, 1991, please amend the above-identified application as follows:

IN THE CLAIMS:

Cancel claims 13-17.

REMARKS

The applicant respectfully requests reconsideration.

The claims stand rejected as obvious from the disclosure of the cited Vogelsang, et al. patent in view of the art admitted in the specification. The claims relate to administration of azelastine directly into nasal and eye tissues.

It is not clear what aspects of the art admitted in the specification is the basis of the examiner's reference, but the introductory passage on page 1 simply mentions to the fact that azelastine has anti-allergic and anti-histamine properties. However, this information does not imply a mode of administration, although, as shown below, the customary mode of administration for such medications is systemic (e.g., oral or injection). Further, as the cited Vogelsang patent refers to the fact that its compounds are used for

060 MC 01/17/92 07551644 1 116 350.00 CK

the treatment of histamine induced disturbances (see Abstract, Column 1) and allergies (Column 6, line 72), it is not seen where the above cited passage adds anything to the disclosure of the Vogelsang patent. The Examiner has referred on page 3 of the Office Action to the use of "preseruahres" (sic) in this connection, but this comment is not understood. Therefore, it is the disclosure of the Vogelsang patent which is the focus of the following remarks.

In his discussion of this patent, on page 3 of the Office Action, the Examiner has referred to column 43 lines 5-15 of Vogelsang, but this comment also is not understood. There is no column 43 in this patent.

The only information in the Vogelsang patent on mode of administration is in the paragraph bridging columns 6 and 7, viz.

> The compounds according to the present invention are used as active ingredients in pharmaceutical preparations and may be administered in usual embodiments such as tablets, dragees, capsules, suppositories, drops, ointments, creams as well as injection solutions. They are in particular used for the treatment of the various forms of allergies. Thus, they have been used successfully in humans in the treatment of asthma bronchiale, for the treatment of various disorders of the skin and mucous membranes hay fever and rhinitis vasmotorica. In general, they are administered in such treatments in a dosage of 0.4 to 4 mg. per day and human patient. The symptoms of the above allergic diseases may be effectively reduced upon a single dose for up to 24 hours. The effectiveness of the components of the present invention in humans which is produced very rapidly and over a prolonged period of time in comparison to other antihistamines, may be particularly well shown in the reduction of the size of an artificially produced lesion by means of a histamine liberator according to L. Kerp, H. Kasimiar, P.N. Tie, Med. Welt 17 NF 2794 (1966). The

> compounds according to the present invention may be used as such or in combination with other active ingredients as they are usual in antihistaminic preparations.

The portion which has been underlined appears to be the sole basis for the rejection, and more particularly the disclosure that the compounds "may be administered in...drops..." To this, the Examiner has added the following comment:

> It would have been obvious to administer the azelastine composition of Vogelsang directly to the nasal tissues or conjunctival sac...<u>because these are the areas to which medicament drops are normally applied</u>."

However, the Examiner has indulged in a leap of logic which is not supported by the reference in making this comment. The reference does not say that drops are administered to the patient. It merely says that the compounds may be administered in drops. Thus, a medicine dropper is a well known device for measuring liquids. See for example page 1329 in the attached extract from *The United States Pharmacopoeia* which describes the use of a medicine dropper and its ability to deliver a measured quantity of liquid, with various degrees of precision. But there is no indication of where the drops are to be delivered. For example, a medicine dropper is used as a means of delivering a measured quantity of a concentrated liquid to water which is to be swallowed or used as a mouthwash.

The Examiner has cited no reference to support his contention that "the nasal tissues or conjuctival sac...are the areas to which medicament drops are normally applied." However, such a sweeping statement, which provides the sole link between the Vogelsang patent and the present invention, should be supported by a reference.

Referring again to the attached extract from *The United States Pharmacopoeia* , it will be noted that various modes of administration are discussed. Compositions which are intended to be administered to the nose are referred to as "Nasal Solutions" and compounds which are administered to the eye are referred to as "Ophthalmic Solutions", see pages 1655 and 1338. On the other form, among the forms of medicine which are described, the word "drops" does not appear as a form of material to be administered to the eyes or nasal passages.

Similarly, the words "ointment" and "cremes" are used in the reference, and these are mentioned in the attached copy of an extract from Remington's *Pharmaceutical Sciences*. See pages 1594 and 1616. However, there is no indication of direct application to nasal passages and eyes.

Finally, there is attached a copy of an extract from *Drug Facts and Comparisons*. While numerous antihistamines are mentioned, and modes of administration are described, there is no suggestion of direct application to the eyes and nasal passages. Dosage forms such as capsules, tablets, injections, suppositories, elixirs and syrups are described, but none for direct application to the eyes and nasal passages.

Therefore, the only link between the present invention and the cited Vogelsang reference is the Examiner's interpretation of the word "drops" in this patent, and the Examiner's unsubstantiated comment that "the nasal tissues or conjunctival sac...are the areas to which medicament drops are normally applied." However, as indicated above, such a sweeping statement, providing the sole link between the reference and the present invention and the cited patent,

ought to be supported by a reference. Since none has been cited, it is submitted that the claims should be allowed.

Further, applicant submits that the Examiner should consider the decision in the case of Ex parte Keith, 154 USPQ 320, which held:

> Asserted inherency must be a necessary result and not merely a possible result. Ex parte Vander Wal et al., 705 O.G. 5, 1956 USPQ 11, 109 USPQ 119, and decisions cited therein.

Here, the Examiner reasons that the only possible meaning of the reference to "drops" in the reference is that they are to be applied directly to the eyes and nasal passages. However, the Examiner has not shown, by citation of a reference, or in any other way, that this is the only possible meaning of the word "drops." Rather, a medicine dropper is simply a device for measuring a liquid. While droppers are used to administer liquid medications to eyes and nasal passages, this does not mean that this mode of administration is the "necessary" and only "possible" inference to be drawn from the reference to "drops" in the cited patent.

For these reasons, it is submitted that the claims are patentable and that they should be allowed.

Respectfully submitted,
CUSHMAN, DARBY & CUSHMAN

By _____
Lawrence A. Hymo
Reg. No. 19,057

1615 L Street N.W.
Washington, D.C. 20036

Telephone (202) 861-3000

IN THE UNITED S. ES PATENT AND TRADEMARK (ICE

re PATENT APPLICATION of
ventor(s): HETTCHE, Helmut

pln No.: 0 7 / 551,644
eries code † serial no.

Filed July 2, 1990

Title: AZELASTINE-CONTAINING MEDICAMENTS

Comm. and Mail
BOX AF

PATENT APPLICATION

Group Art Unit 152

Examiner L. Piccone

Atty. Dkt. 62748 / 87-217 PH
M# / Client Ref.
(Our Deposit Account No. 03-3975)
(Our Order No. 326 / 62748
C# / M#

Date: January 15, 1992
Response Under 37 CFR 1.116
Expedited Procedure
Examining Group 152

RECEIVED
JAN 22 1992
GROUP 150

on. Commissioner of Patents and Trademarks
ashington, D.C. 20231

ir:

RESPONSE/AMENDMENT/LETTER

This is a response/amendment/letter in the above-identified application and includes the erewith attachment of same date and subject which is incorporated hereinto by reference and the ignature below is to be treated as the signature to the attachment in absence of a signature hereto.

FEE REQUIREMENTS FOR CLAIMS AS AMENDED

1. "Small Entity" statement(s) filed	Claims remaining after amendment	Highest number previously paid for	Present Extra	Additional Fee
[ ] previously				
[ ] herewith(___(No.))				
Total Effective Claims	* 18	minus ** 20	= ____	X $20/$10 = $____
Independent Claims	* 7	minus *** 7	= ____	X $72/$36 = $____

Large/Small Entity

If amendment enters proper multiple dependent claim(s) into this application for first time(leave blank if this is a reissue appln)add $220/$110 +____

Original due date: [ ] None; [x] (date) December 12, 1991

Petition is hereby made to extend the original due date to cover the date this response is filed for which the requisite fee is attached (Large/Small Entity: 1 month $110/$55; 2 months $350/$175; 3 months $810/$405): +350.00

If Terminal Disclaimer attached, add Rule 20(d) Official fee ($110/$55)- - - - - +____

Enter any previous extension fee paid since above original due date (item 5) and subtract -____

Subtotal $350.00

TOTAL FEE ATTACHED $350.00

*If the entry in this space is less than entry in the next space, the "Present Extra" result is "0".
**If the "Highest number previously paid for" in this space is less than 20, write "20" in this space.
***If the "Highest number previously paid for" in this space is less than 3, write "3" in this space.

HARGE STATEMENT: The Commissioner is hereby authorized to charge any fee specifically authorized hereafter, or any missing or insufficient fee(s) filed, asserted to be filed, or which should have been filed herewith or concerning any paper filed hereafter, and which may be required under Rules 16-18 (missing insufficiencies only) now or hereafter relative to this application and the resulting Official Document under Rule 20, or credit any overpayment, to our count/Order Nos. shown in the heading hereof, for which purpose a duplicate copy of this sheet is attached.

his CHARGE STATEMENT does not authorize charge of the issue fee until/unless an issue fee ransmittal sheet is filed.

Query: Is appeal deadline now? If so, file Notice of Appeal separately.

515 L Street N.W.
leventh Floor
ashington, D.C. 20036-5601
el: (202) 861-3000
tty/Sec: LAH/mey

CUSHMAN, DARBY & CUSHMAN
By Atty: Lawrence A. Hymo
Sig: _____

Reg. No. 19,057
Fax: (202) 822-0944
Tel.: (202) 861-3015

DC-120 4/91 NOTE: File this cover sheet in duplicate with post card receipt (CDC-103) and attachments

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
07/551,644	07/12/90	HETTICHE H	62748/87217P

CUSHMAN, DARBY & CUSHMAN
ELEVENTH FLOOR
1615 L STREET, N.W.
WASHINGTON, DC 20036-5601

EXAMINER	
PICCONE, L	
ART UNIT	PAPER NUMBER
1502	16

DATE MAILED: 01/30/92

Below is a communication from the EXAMINER in charge of this application

COMMISSIONER OF PATENTS AND TRADEMARKS

ADVISORY ACTION

☒ THE PERIOD FOR RESPONSE:

a) ☒ is extended to run _____ or continues to run 5 Months from the date of the final rejection

b) ☐ expires three months from the date of the final rejection or as of the mailing date of this Advisory Action, whichever is later. In no event however, will the statutory period for the response expire later than six months from the date of the final rejection.

Any extension of time must be obtained by filing a petition under 37 CFR 1.136(a), the proposed response and the appropriate fee. The date on which the response, the petition , and the fee have been filed is the date of the response and also the date for the purposes of determining the period of extension and the corresponding amount of the fee. Any extension fee pursuant to 37 CFR 1.17 will be calculated from the date of the originally set shortened statutory period for response or as set forth in b) above.

☐ Appellant's Brief is due in accordance with 37 CFR 1.192(a).

☒ Applicant's response to the final rejection, filed 11/5/92 has been considered with the following effect, but it is not deemed to place the application in condition for allowance:

1. ☒ The proposed amendments to the claim and /or specification will not be entered and the final rejection stands because:

   a. ☒ There is no convincing showing under 37 CFR 1.116(b) why the proposed amendment is necessary and was not earlier presented.

   b. ☐ They raise new issues that would require further consideration and/or search. (See Note).

   c. ☐ They raise the issue of new matter. (See Note).

   d. ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal.

   e. ☐ They present additional claims without cancelling a corresponding number of finally rejected claims.

   NOTE: _____

2. ☐ Newly proposed or amended claims _____ would be allowed if submitted in a separately filed amendment cancelling the non-allowable claims.

3. ☒ Upon the filing an appeal, the proposed amendment ☒ will be entered ☐ will not be entered and the status of the claims will be as follows:

   Claims allowed: _____
   Claims objected to: _____
   Claims rejected: 1-12

   However;

   ☐ Applicant's response has overcome the following rejection(s): _____

4. ☐ The affidavit, exhibit or request for reconsideration has been considered but does not overcome the rejection because _____

5. ☐ The affidavit or exhibit will not be considered because applicant has not shown good and sufficent reasons why it was not earlier presented.

☐ The proposed drawing correction ☐ has ☐ has not been approved by the examiner.

☐ Other

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
ART UNIT 152

MP0108

260.00 119 Gp 152

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Re: Appeal to The Board of Patent Appeals and Interferences

PATENT APPLICATION

In re PATENT APPLICATION of
Inventor(s): HETTCHE, Helmut
Appln. No.: 0 7 / 551,644
series code † † serial no.

Filed: November 12, 1991

Title: AZELASTINE-CONTAINING MEDICAMENTS

Group Art Unit: 152
Examiner: L. Piccone

(Our Deposit Account No. 03-3975
(Our Order No. 326 / 62748
C# / M#
Atty. Dkt. 62748 / 87-217 PH
M# / Client Ref.
Date: February 12, 1992

T/Appeal
D.C.
2/25/92

Hon. Commissioner of Patents and Trademarks
Washington, D.C. 20231
Sir:

1. [X] **NOTICE OF APPEAL**: Applicant hereby appeals to the Board of Patent Appeals and Interferences from the decision (not Advisory Action) dated September 12, 1991 of the Examiner twice/finally rejecting claims 1 - 18.

2. [ ] **BRIEF** on appeal in this application is attached in triplicate.

3. [ ] An **ORAL HEARING** is respectfully requested under Rule 194 (due one month after Examiner's Answer or three months after filing a reply to new ground rejection in Examiner's Answer. Neither due date is extendable).

4. [ ] Reply Brief (only to new point(s) of argument, Rule 193(b)) is attached in triplicate.

5. [ ] Reply Brief (on new ground(s) of rejection, Rule 193(b)) is attached in triplicate.

6. [ ] "Small entity" verified statement filed: [ ] herewith. [ ] previously.

7. **FEE CALCULATION:**

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FEB 21 1992
GROUP 150

Fees

	Large/Small Entity	
If box 1 above is X'd,	enter $260/$130*	$ 260.00
If box 2 above is X'd,	enter $260/$130*	$
If box 3 above is X'd,	enter $260/$130*	$
If box 4 or 5 above is X'd,	enter -0- (no fee)	$

8. Original due date: December 12, 1991

9. **Petition is hereby made** to extend the original due date to cover the date of this paper and any enclosure for which the requisite fee is (Large/Small Entity: 1 month $110/$55; 2 months $350/$175; 3 months $810/$405; 4 months $1,280/$640) + 350.00

10. **Subtotal** $ 610.00

11. Enter amount of extension fee paid [ ] previously since above original due date (item 8) [X] with concurrently filed amendment - and subtract 350.00

12. **TOTAL FEE** $ 260.00

13. [ ] Fee Attached

14. [ ] *Fee NOT required since paid in prior appeal in which the Board of Patent Appeals and Interferences did not render a decision on the merits.

CHARGE STATEMENT: The Commissioner is hereby authorized to charge any fee specifically authorized hereafter, or any missing or insufficient fee(s) filed, or asserted to be filed, or which should have been filed herewith or concerning any paper filed hereafter, and which may be required under Rules 16-18 (missing or insufficient fee only) now or hereafter relative to this application and the resulting Official document under Rule 20, or credit any overpayment, to our Account/Order Nos. shown in the heading hereof for which purpose a duplicate copy of this sheet is attached. **This CHARGE STATEMENT does not authorize charge of the issue fee until/unless an issue fee transmittal form is filed.**

1615 L Street, N.W.
Eleventh Floor
Washington, D.C. 20036-5601
Tel: (202) 861-3000
Atty/Sec: LAH/mey

CUSHMAN, DARBY & CUSHMAN
By Atty: Lawrence A. Hymo Reg. No. 19,057
Sig:
Fax: (202) 822-0944
Tel.: (202) 861-3015

100 DH 02/20/92 07551644 1 119 260.00 CK

CDC-126 12/91

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re PATENT Application of

Helmut HETTCHE, et al.

Serial No. 07/551,644 Group Art Unit: 1502

Filed: July 12, 1990 Examiner: L. Piccone

For: AZELASTINE-CONTAINING MEDICAMENTS

April 27, 1992

RECEIVED
APR 29 1992
GROUP 150

* * * * * * * *

#18
D. Gassaway
4-30-92

Hon. Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Sir:

In connection with the above application, we enclose, for the Examiner's consideration, a copy of the Search Report of the European Patent Office, in connection with a counterpart of the present application. We also enclose copies of the two cited documents, German Patents DE 2 164 058 and DE 3 530 793, as well as English language counterparts, British Patent 1,377,231 and U.S. Patent 4,704,387. The European Search Report identifies the parts of the German citations which the searcher thought were pertinent. ("Seite" means "page", "Zeile" means "line", "Beispiel" means "Example").

Respectfully submitted,
CUSHMAN, DARBY & CUSHMAN

By _____
Lawrence A. Hymo
Reg. No. 19,057

1615 L Street N.W.
Washington, D.C. 20036

Tel. (202) 861-3015

MP0110

DATE: April 27, 1992 Sheet 1 of 1

Form PTO-1449 (REV. 2-83) Cushman Version — U.S. Department of Commerce Patent and Trademark Office

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use several sheets if necessary)

ATTY. DOCKET NO.	GROUP ART UNIT
62748 / 87 217 PH MF / Client Ref.	1502
APPLICANT (Inventor(s)) HETTCHE, et al.	EXAMINER L. Piccone
APPLN. NO. 0 7/551,644	FILING DATE July 12, 1990

RECEIVED
APR 29 1992
GROUP 150

U.S. PATENT DOCUMENTS

*Examiner's Initials		Document Number	Date Mo/Yr	Name (Family Name of First Inventor)	Class	Subclass	Filing Date If Appropriate
[redacted]	AR	4 7 0 4 3 8 7	11/87	ENGEL et al.	514	212	
	BR						
	CR						
	DR						
	ER						
	FR						
	GR						
	HR						
	IR						
	JR						
	KR						
	LR						
	MR						

MAIL ROOM 47 APR 29 1992 PAT & TRADE MARK OFF.

FOREIGN PATENT DOCUMENTS

		Document Number	Date Mo/Yr	Country	English Abstract Enclosed	English Abstract No	Class	Subclass	Translation Readily Available Enclosed	Translation Readily Available No
N.L.	NR	2 1 6 4 0 5 8	7/1972	Germany DEX		X	546	133		
N.L.	OR	3 5 3 0 7 9 3	3/86	Germany DEX		X	514	212		
N.L.	PR	1 3 7 7 2 3 1	1/1972	England GBX		X	—	—		
	QR									
	RR									
	SR									

OTHER DOCUMENTS (Including in this order Author, Title, Periodical Name, Date, Pertinent Pages, Etc.)

1. N.L.	TR	European Search Report
	UR	
	VR	

EXAMINER Neil Levy DATE CONSIDERED 6/8/92

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

CDC-1449 2/90(PC)

110.00, 15 260.00 x 0 N 64/152

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re PATENT Application of

Helmut HETTCHE

Serial No. 07/551,664 Group Art Unit: 152

Filed: July 12, 1992 Examiner: L. Piccone

For: AZELASTINE-CONTAINING MEDICAMENTS

19/EXT (1) & Brief

April 28, 1992

Dell 5/11/92

BRIEF FOR THE APPLICANT

Hon. Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Sir:

This is an appeal from the final rejection of claims 1-12 and 18.

STATUS OF CLAIMS

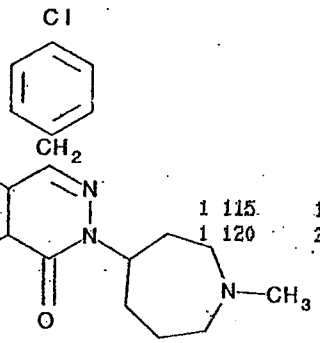
The application originally contained claims 1-18. Claims 13-17 have been cancelled, leaving claims 1-12 and 18, which are presented in this appeal.

STATUS OF AMENDMENTS

An amendment was submitted after the final rejection, cancelling claims 13-17. It has been entered.

SUMMARY OF THE INVENTION

The invention relates to a new use of azelastine, a phthalazinone derivative having the formula:



120 WP 05/07/92 07551644
120 WP 05/07/92 07551644
1 115 110.00 CK
1 120 260.00 CK

Azelastine has been used in prophylactic treatment of asthma and for its anti-allergic and antihistamine properties.

The present invention is based on a surprising discovery that azelastine and its physiologically acceptable salts display advantageous and surprising effects when applied directly in the nose and/or to the conjunctival sac of the eye. This treatment produces elimination or marked relief in allergy-related rhinitis, the common cold, and vasomotor cold. Further, application directly in the nose has been found to have advantageous effects on the mucous membrane of the eye.

The invention is claimed in claim 1 as a method which comprises *applying* azelastine *directly to the nasal tissues or to the conjunctival sac of the eye.* Claims 2-8 relate to more preferred features of the pharmaceutical composition containing azelastine which is applied in accordance with the method of claim 1. Claims 9-11 relate to more preferred modes of application of the azelastine-containing composition. Claim 12 is similar to claim 1, in defining a method of treatment with azelastine. However, it defines the symptoms which are treated more specifically than in claim 1, i.e., "a patient suffering from allergy-related or vasomotor or rhino virus-related colds or symptoms."

Claim 18 relates to a novel composition containing azelastine which is useful for the present invention. More specifically, Claim 18 relates to a powder containing azelastine and an appropriate pharmaceutical solid carrier.

ISSUES

The Examiner has rejected claims 1-12 and 18 as obvious under 35 U.S.C. § 103 over Vogelsang, U.S. Patent 3,813,384 "in view of art admitted in the specification." The Examiner separately rejected claims 13-17. However, since those claims have been cancelled, it is assumed that the

grounds of rejection applied against those claims are no longer at issue.

GROUPING OF CLAIMS

The Examiner has grouped claims 1-12 and 18 together. However, applicants believe that claims 1-12 should be considered separately from claim 18.

ARGUMENT

Claims 1-12 and 18 stand rejected as obvious from the disclosure of the cited Vogelsang, et al. patent in view of "the art admitted in the specification." The claims relate to administration of azelastine directly into nasal and eye tissues.

It is not clear what aspects of the art admitted in the specification is the basis of the examiner's reference, but the introductory passage on page 1 simply mentions to the fact that azelastine has anti-allergic and anti-histamine properties. This information does not imply a mode of administration, although, as shown below, the customary mode of administration for such medications is systemic (e.g., oral or injection). Further, as the cited Vogelsang patent refers to the fact that its compounds are used for the treatment of histamine induced disturbances (see Abstract, Column 1) and allergies (Column 6, line 72), it is not seen where the above cited passage adds anything to the disclosure of the Vogelsang patent. The Examiner has referred on page 3 of the Office Action to the use of "preseruahres" (sic) in this connection, but this comment is not understood. Therefore, it is the disclosure of the Vogelsang patent which is the focus of the following remarks.

In his discussion of this patent, on page 3 of the Final Rejection, the Examiner has referred to column 43 lines 5-15 of Vogelsang, but this comment also is not understood. There is no column 43 in this patent.

The only information in the Vogelsang patent on mode of administration is in the paragraph bridging columns 6 and 7, viz.

> The compounds according to the present invention are used as active ingredients in pharmaceutical preparations and may be administered in *usual embodiments such as tablets, dragees, capsules, suppositories, drops, ointments, creams as well as injection solutions*. They are in particular used for the treatment of the various forms of allergies. Thus, they have been used successfully in humans in the treatment of asthma bronchiale, for the treatment of various disorders of the skin and mucous membranes hay fever and rhinitis vasmotorica. In general, they are administered in such treatments in a dosage of 0.4 to 4 mg. per day and human patient. The symptoms of the above allergic diseases may be effectively reduced upon a single dose for up to 24 hours. The effectiveness of the components of the present invention in humans which is produced very rapidly and over a prolonged period of time in comparison to other antihistamines, may be particularly well shown in the reduction of the size of an artificially produced lesion by means of a histamine liberator according to L. Kerp, H. Kasimiar, P.N. Tie, Med. Welt 17 NF 2794 (1966). The compounds according to the present invention may be used as such or in combination with other active ingredients as they are usual in antihistaminic preparations.

The portion which has been shown in italics above appears to be the sole basis for the rejection, and more particularly the disclosure that the compounds "may be administered in...drops..." To this, the Examiner has added the following comment:

> It would have been obvious to administer the azelastine composition of Vogelsang directly to the nasal tissues or conjunctival sac...because these are the areas to which medicament drops are normally applied.

However, the Examiner has indulged in a leap of logic which is not supported by the reference in making this comment. The reference does not say that drops are administered to the patient. It merely says that the compounds may be administered in drops. Thus, a medicine dropper is a

well known device for measuring liquids. See for example page 1329 in the attached extract from *The United States Pharmacopoeia* which describes the use of a medicine dropper and its ability to deliver a measured quantity of liquid, with various degrees of precision. But there is no indication of where the drops are to be delivered. For example, a medicine dropper is used as a means of delivering a measured quantity of a concentrated liquid to water which is to be swallowed or used as a mouthwash.

The Examiner has cited no reference to support his contention that "the nasal tissues or conjunctival sac...are the areas to which medicament drops are normally applied." However, such a sweeping statement, which provides the sole link between the Vogelsang patent and the present invention, should be supported by a reference.

Referring again to the attached extract from *The United States Pharmacopoeia*, it will be noted that various modes of administration are discussed. Compositions which are intended to be administered to the nose are referred to as "Nasal Solutions" and compounds which are administered to the eye are referred to as "Ophthalmic Solutions", see pages 1655 and 1338. On the other hand, among the forms of medicine which are described, the word "drops" does not appear as a form of material to be administered to the eyes or nasal passages.

Similarly, the words "ointment" and "cremes" are used in the reference, and these are mentioned in the attached copy of an extract from Remington's *Pharmaceutical Sciences*. See pages 1594 and 1616. However, there is no indication of direct application to nasal passages and eyes.

Finally, there is attached a copy of an extract from *Drug Facts and Comparisons*. While numerous antihistamines are mentioned, and modes of administration are described, there is no suggestion of direct application to the eyes and

nasal passages. Dosage forms such as capsules, tablets, injections, suppositories, elixirs and syrups are described, but none for direct application to the eyes and nasal passages.

Therefore, the only link between the present invention and the cited Vogelsang reference is the Examiner's interpretation of the word "drops" in this patent, and the Examiner's unsubstantiated comment that "the nasal tissues or conjunctival sac...are the areas to which medicament drops are normally applied." However, as indicated above, such a sweeping statement, providing the sole link between the reference and the present invention and the cited patent, ought to be supported by a reference. Since none has been cited, it is submitted that the claims should be allowed.

Further, applicant requests that the Board consider the decision in the case of *Ex parte Keith*, 154 USPQ 320, which held:

> Asserted inherency must be a necessary result and not merely a possible result. Ex parte Vander Wal et al., 705 O.G. 5, 1956 USPQ 11, 109 USPQ 119, and decisions cited therein.

Here, the Examiner reasons that the only possible meaning of the reference to "drops" in the reference is that they are to be applied directly to the eyes and nasal passages. However, the Examiner has not shown, by citation of a reference, or in any other way, that this is the only possible meaning of the word "drops." Rather, a medicine dropper is simply a device for measuring a liquid. While droppers are used to administer liquid medications to eyes and nasal passages, this does not mean that this mode of administration is the "necessary" and only "possible" inference to be drawn from the reference to "drops" in the cited patent.

The foregoing comments are applicable to both claims 1-12 and claim 18. However, the following additional com-

ments are thought to be appropriate specifically to claim 18.

Claim 18 relates to a powder containing azelastine and a pharmaceutical carrier. Powders are not among the materials mentioned in the cited Vogelsang patent, and so this claim is clearly patentable.

CONCLUSION

For these reasons, it is submitted that the claims are patentable and that they should be allowed.

Respectfully submitted,
CUSHMAN, DARBY & CUSHMAN

By _____
Lawrence A. Hymo
Reg. No. 19,057

1615 L Street N.W.
Washington, D.C. 20036

Tel. (202) 861-3015

APPENDIX

THE CLAIMS

1. A method for the treatment of irritation or disorders of the nose and eye which comprises applying directly to nasal tissues or to the conjunctival sac of the eye a medicament which contains a member selected from the group consisting of azelastine and its physiologically acceptable salts.

2. A method as set forth in claim 1 in which the medicament contains 0.0005 to 2% (weight/weight) of azelastine or an amount of a physiologically acceptable salt of azelastine which contains 0.0005 to 2% (weight/weight) azelastine.

3. A method as set forth in claim 2 in which the medicament contains 0.001 to 1% (weight/weight) of azelastine or an amount of a physiologically acceptable salt of azelastine which contains 0.001 to 1% (weight/weight) azelastine.

4. A method as set forth in claim 1 in which the medicament contains 0.003 to 0.5% (weight/weight) of azelastine or an amount of a physiologically acceptable salt of azelastine which contains 0.003 to 0.5% (weight/weight) azelastine.

5. A method as set forth in claim 1 in which the medicament contains a pharmaceutically usable preservative in an amount of 0.001 to 0.1%.

6. A method as set forth in claim 1 in which the medicament is a solution.

7 A method as set forth in claim 1 in which the medicament is an aqueous solution.

8. A method as set forth in claim 1 in which the medicament is a solution which contains 0.001 to 0.05% (weight/volume of solution) of sodium-2-(ethylmercurithio)-benzoate or 0.001 to 0.1%

(weight/volume of solution) of alkylbenzyldimethyl ammonium chloride.

9. A method as set forth in claim 1 in which the medicament is applied by spraying.

10. A method as set forth in claim 1 in which the medicament is applied as drops.

11. A method as set forth in claim 1 in which the medicament is a powder.

12. A method for the treatment of a patient suffering from allergy-related, or vasomotor or rhino-related colds or symptoms which comprises applying directly to the patient's nasal tissues or to the conjunctival sac of the patient's eye a medicament which contains a member selected from the group consisting of azelastine and its physiologically acceptable salts.

18. Powder containing 0.0005 to 2% of azelastine or a physiologically acceptable salt of azelastine as active agent together with conventional pharmaceutical carrier substances.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE PATENT
Re: Appeal to The Board of Patent Appeals and Interferences APPLICATION

In re PATENT APPLICATION of
Inventor(s): HETTCHE, Helmut
Appln. No.: 0 7 / 551,644
series code † † serial no.

Filed: November 12, 1991

Title: AZELASTINE-CONTAINING MEDICAMENTS

Group Art Unit: 152
Examiner: L. Piccone

RECEIVED
MAY 0 8 1992
GROUP 150

(Our Deposit Account No. 03-3975
(Our Order No. 326 / 62748
C# / M#
Atty. Dkt. 62748 / 87-217 PH
M# / Client Ref.

Date: April 28, 1992

Hon. Commissioner of Patents and Trademarks
Washington, D.C. 20231
Sir:

1. [ ] **NOTICE OF APPEAL**: Applicant hereby appeals to the Board of Patent Appeals and Interferences from the decision (not Advisory Action) dated September 12, 1991 of the Examiner twice/finally rejecting claims 1 - 18.

2. [X] **BRIEF** on appeal in this application is attached in triplicate.

3. [ ] An **ORAL HEARING** is respectfully requested under Rule 194 (due one month after Examiner's Answer or three months after filing a reply to new ground rejection in Examiner's Answer. Neither due date is extendable).

4. [ ] Reply Brief (only to new point(s) of argument, Rule 193(b)) is attached in triplicate.

5. [ ] Reply Brief (on new ground(s) of rejection, Rule 193(b)) is attached in triplicate.

6. [ ] "Small entity" verified statement filed: [ ] herewith. [ ] previously.

7. **FEE CALCULATION:**

Fees

	Large/Small Entity	
If box 1 above is X'd,	enter $260/$130*	$
If box 2 above is X'd,	enter $260/$130*	$ 260.00
If box 3 above is X'd,	enter $220/$110*	$
If box 4 or 5 above is X'd,	enter -0- (no fee)	$

8. Original due date: April 12, 1992

9. **Petition is hereby made** to extend the original due date to cover the date of this paper and any enclosure for which the requisite fee is (Large/Small Entity: 1 month $110/$55; 2 months $350/$175; 3 months $810/$405; 4 months $1,280/$640) + 110.00

10. **Subtotal** $370.00

11. Enter amount of extension fee paid [ ] previously since above original due date (item 8) [ ] with concurrently filed amendment ---------- and subtract

12. **TOTAL FEE** $ 370.00

13. [X] Fee Attached

14. [ ] *Fee NOT required since paid in prior appeal in which the Board of Patent Appeals and Interferences did not render a decision on the merits.

CHARGE STATEMENT: The Commissioner is hereby authorized to charge any fee specifically authorized hereafter, or any missing or insufficient fee(s) filed, or asserted to be filed, or which should have been filed herewith or concerning any paper filed hereafter, and which may be required under Rules 16-18 (missing or insufficient fee only) now or hereafter relative to this application and the resulting Official document under Rule 20, or credit any overpayment, to our Account/Order Nos. shown in the heading hereof for which purpose a duplicate copy of this sheet is attached. **This CHARGE STATEMENT does not authorize charge of the issue fee until/unless an issue fee transmittal form is filed.**

CUSHMAN, DARBY & CUSHMAN

1615 L Street, N.W.
Eleventh Floor
Washington, D.C. 20036-5601
Tel: (202) 861-3000
Atty/Sec: LAH/mey

By Atty: Lawrence A. Hymo Reg. No. 19,057

Sig: 

Fax: (202) 822-0944
Tel.: (202) 861-3015

CDC-126 12/91

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
07/551,644	07/12/90	HETTCHE H	62748/87217P

CUSHMAN, DARBY & CUSHMAN
ELEVENTH FLOOR
1615 L STREET, N.W.
WASHINGTON, DC 20036-5601

EXAMINER	
LEVY, N	

ART UNIT	PAPER NUMBER
1502	20

DATE MAILED: 06/30/92

NOTICE OF ALLOWABILITY

PART I.

1. ☒ This communication is responsive to Brief, 4/28/92
2. ☒ All the claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice Of Allowance And Issue Fee Due or other appropriate communication will be sent in due course.
3. ☒ The allowed claims are 1-12
4. ☐ The drawings filed on _____ are acceptable.
5. ☒ Acknowledgment is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☒ been received. ☐ been received. ☐ been filed in parent application Serial No. _____, filed on _____
6. ☒ Note the attached Examiner's Amendment.
7. ☐ Note the attached Examiner Interview Summary Record, PTOL-413.
8. ☐ Note the attached Examiner's Statement of Reasons for Allowance.
9. ☐ Note the attached NOTICE OF REFERENCES CITED, PTO-892.
10. ☒ Note the attached INFORMATION DISCLOSURE CITATION, PTO-1449.

PART II.

A SHORTENED STATUTORY PERIOD FOR RESPONSE to comply with the requirements noted below is set to EXPIRE THREE MONTHS FROM THE "DATE MAILED" indicated on this form. Failure to timely comply will result in the ABANDONMENT of this application. Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

1. ☐ Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL APPLICATION, PTO-152, which discloses that the oath or declaration is deficient. A SUBSTITUTE OATH OR DECLARATION IS REQUIRED.
2. ☐ APPLICANT MUST MAKE THE DRAWING CHANGES INDICATED BELOW IN THE MANNER SET FORTH ON THE REVERSE SIDE OF THIS PAPER.
   a. ☐ Drawing informalities are indicated on the NOTICE RE PATENT DRAWINGS, PTO-948, attached hereto or to Paper No. _____. _____ CORRECTION IS REQUIRED.
   b. ☐ The proposed drawing correction filed on _____ has been approved by the examiner. CORRECTION IS REQUIRED.
   c. ☐ Approved drawing corrections are described by the examiner in the attached EXAMINER'S AMENDMENT. CORRECTION IS REQUIRED.
   d. ☐ Formal drawings are now REQUIRED.

Any response to this letter should include in the upper right hand corner, the following information from the NOTICE OF ALLOWANCE AND ISSUE FEE DUE: ISSUE BATCH NUMBER, DATE OF THE NOTICE OF ALLOWANCE, AND SERIAL NUMBER.

Attachments:

- ✓ Examiner's Amendment
- — Examiner Interview Summary Record, PTOL-413
- — Reasons for Allowance
- — Notice of References Cited, PTO-892
- ✓ Information Disclosure Citation, PTO-1449
- — Notice of Informal Application, PTO-152
- — Notice re Patent Drawings, PTO-948
- — Listing of Bonded Draftsmen
- — Other

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
ART UNIT 152

MP0122

PTOL-37 (REV. 4-89) *

USCOMM-DC 89-3789

An Examiner's Amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 C.F.R. § 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the Issue Fee.

Cancel claim 18.

Authorization for this Examiner's Amendment was given in a telephone interview with attorney Hymo on 06/08/92.

Any inquiry concerning this communication should be directed to Neil Levy at telephone number (703) 308-2351.

N. Levy:dl
June 25, 1992

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
ART UNIT 152

6.

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office

Address: Box ISSUE FEE
COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

CUSHMAN, DARBY & CUSHMAN
ELEVENTH FLOOR
1615 L STREET, N.W.
WASHINGTON, DC 20036-5601

NOTICE OF ALLOWANCE AND ISSUE FEE DUE

] Note attached communication from the Examiner
] This notice is issued in view of applicant's communication filed _____

SERIES CODE/SERIAL NO.	FILING DATE	TOTAL CLAIMS	EXAMINER AND GROUP ART UNIT	DATE MAILED
07/551,644	07/12/90	012	LEVY, N 1502	06/30/92

First Named Applicant HETTCHE, HELMUT

TLE OF VENTION AZELASTINE CONTAINING MEDICAMENTS

	ATTY'S DOCKET NO.	CLASS-SUBCLASS	BATCH NO.	APPLN. TYPE	SMALL ENTITY	FEE DUE	DATE DUE
1	62748/87217P	424-489.000	E21	UTILITY	NO	$1130.00	09/30/92

HE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. ROSECUTION ON THE MERITS IS CLOSED.

E ISSUE FEE MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS PLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED.

OW TO RESPOND TO THIS NOTICE:

Review the SMALL ENTITY Status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the Status is changed, pay twice the amount of the FEE DUE shown above and notify the Patent and Trademark Office of the change in status, or
B. If the Status is the same, pay the FEE DUE shown above.

If the SMALL ENTITY is shown as NO:

A. Pay FEE DUE shown above, or
B. File verified statement of Small Entity Status before, or with, payment of 1/2 the FEE DUE shown above.

Part B of this notice should be completed and returned to the Patent and Trademark Office (PTO) with your ISSUE FEE. Even if the ISSUE FEE has already been paid by a charge to deposit account, Part B should be completed and returned. If you are charging the ISSUE FEE to your deposit account, Part C of this notice should also be completed and returned.

All communications regarding this application must give series code (or filing date), serial number and batch number. Please direct all communications prior to issuance to Box ISSUE FEE unless advised to the contrary.

PORTANT REMINDER: Patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees.

85 (REV 12-88)(OMB Clearance is pending) PATENT AND TRADEMARK OFFICE COPY

1130-142

PART B - ISSUE FEE TRANSMITTAL

MAILING INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE. Blocks 2 through 6 should be completed where appropriate. All further correspondence including the Issue Fee Receipt, the Patent, advanced orders and notification of maintenance fees will be mailed to addressee entered in Block 1 unless you direct otherwise, by: (a) specifying a new correspondence address in Block 3 below; or (b) providing the PTO with a separate "FEE ADDRESS" for maintenance fee notifications with the payment of Issue Fee or thereafter. **See reverse for Certificate of Mailing.**

PATENT & TRADEMARK OFF. AUG 24 1992

MAIL ROOM AUG 24 1992 PAT. & TRADEMARK OFF.

CORRESPONDENCE ADDRESS

CUSHMAN, DARBY & CUSHMAN
ELEVENTH FLOOR
1615 L STREET, N.W.
WASHINGTON, DC 20036-5601

(202)

2. INVENTOR(S) ADDRESS CHANGE (Complete only if there is a change)

INVENTOR'S NAME
Street Address
City, State and ZIP Code
CO-INVENTOR'S NAME
Street Address
City, State and ZIP Code

☐ Check if additional changes are on reverse side

SERIES CODE/SERIAL NO.	FILING DATE	TOTAL CLAIMS	EXAMINER AND GROUP ART UNIT	DATE MAILED
07/551,644	07/12/90	012	LEVY, N 1502	06/30/92

First Named Applicant: HETTCHE, HELMUT

TITLE OF INVENTION: AZELASTINE CONTAINING MEDICAMENTS

	ATTY'S DOCKET NO.	CLASS-SUBCLASS	BATCH NO.	APPLN. TYPE	SMALL ENTITY	FEE DUE	DATE DUE
1	62748/87217P	424-489.000	E21	UTILITY	NO	$1130.00	09/30/92

Further correspondence to be mailed to the following:

Cushman, Darby & Cushman
1100 New York Avenue
9th Floor
Washington, D.C. 20036

4. For printing on the patent front page, list the names of not more than 3 registered patent attorneys or agents OR alternatively, the name of a firm having as a member a registered attorney or agent. If no name is listed, no name will be printed.

1 Cushman, Darby&Cushman
2
3

060 MC 09/04/92 07551644 DO NOT USE THIS SPACE
01 142 1130.00 CK

SC13268 09/03/92 07551644 03-3975 130 561 30.00CH

ASSIGNMENT DATA TO BE PRINTED ON THE PATENT (print or type)

1) NAME OF ASSIGNEE:
Asta Pharma AG

2) ADDRESS: (City & State or Country)
Germany

3) STATE OF INCORPORATION, IF ASSIGNEE IS A CORPORATION
Germany

This application is NOT assigned.

Assignment previously submitted to the Patent and Trademark Office.

Assignment is being submitted under separate cover. Assignments should be directed to Box ASSIGNMENTS.

PLEASE NOTE: Unless an assignee is identified in Block 5, no assignee data will appear on the patent. Inclusion of assignee data is only appropriate when an assignment has been previously submitted to the PTO or is being submitted under separate cover. Completion of this form is NOT a substitute for filing an assignment.

6a. The following fees are enclosed:
XX Issue Fee ☐ Advanced Order - # of Copies 10

6b. The following fees should be charged to: (Minimum of 10)
DEPOSIT ACCOUNT NUMBER 03-3975
(Enclose Part C) only if deficient or missing
XX Issue Fee ☐ Advanced Order - # of Copies
☐ Any Deficiencies in Enclosed Fees (Minimum of 10)

The COMMISSIONER OF PATENTS AND TRADEMARKS is requested to apply the Issue Fee to the application identified above.

(Signature of party in interest of record) (Date)
Lawrence A. Hymo 19,057 8/31/92

NOTE: The Issue Fee will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the Patent and Trademark Office.

TRANSMIT THIS FORM WITH FEE-CERTIFICATE OF MAILING ON REVERSE

(REV. 12-88) (OMB Clearance is pending)

MP0125

PTO UTILITY GRANT
Paper Number 21

The United States of America

The Commissioner of Patents and Trademarks

Has received an application for a patent for a new and useful invention. The title and description of the invention are enclosed. The requirements of law have been complied with, and it has been determined that a patent on the invention shall be granted under the law.

Therefore, this

United States Patent

Grants to the person or persons having title to this patent the right to exclude others from making, using or selling the invention throughout the United States of America for the term of seventeen years from the date of this patent, subject to the payment of maintenance fees as provided by law.

PATENT AND TRADEMARK OFFICE * UNITED STATES OF AMERICA *

Douglas B. Comer

Acting Commissioner of Patents and Trademarks

Sandra L. Morton

Attest

PTO-1584

7560

#221502

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor : HETTCHE, HELMUT

Application No. : 07/551644

Filing Date : July 12, 1990

Title : AZELASTINE CONTAINING MEDICAMENTS

Office of Publications
Allowed : June 30, 1992

Art Unit : 1500

11/17/92

Date : August 31, 1992

CHANGE OF ADDRESS NOTICE

Hon. Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Sir:

Effective immediately, please change the correspondence address to:

Cushman, Darby & Cushman
Ninth Floor
1100 New York Avenue, N.W.
Washington, D.C. 20005-3918

Our telephone number remains the same: (202) 861-3000. An original, signed notice is on deposit with the PTO Office of Enrollment and Discipline.

Respectfully submitted,

CUSHMAN, DARBY & CUSHMAN

By G. Lloyd Knight
G. Lloyd Knight

Reg. No. : 17698
Fax No. : (202) 822-0944

326 / 62748

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Patent of:	Helmut Hettche
Patent Number:	U.S. 5,164,194
Issued:	November 17, 1992
Expires:	November 17, 2009
FOR:	AZELASTINE CONTAINING MEDICAMENTS

Box Pat. Ext.
Commissioner of Patents and Trademarks
Washington, DC 20231

RECEIVED
DEC 1 8 1996
PATENT EXTENSION
A/C PATENTS

LETTER OF TRANSMITTAL OF
APPLICATION FOR EXTENSION OF PATENT TERM

Dear Sir:

Transmitted herewith is an application for extension of the term of U.S. Patent No. 5,164,194 in accordance with the provisions of 35 U.S.C. 156, a Power of Attorney and Declaration in connection therewith and a duplicate copy of the papers, certified as such.

The filing fee of $1,090.00 required in accordance with 37 C.F.R. Section 120 should be charged to Deposit Account 03-0935. The Commissioner is hereby authorized to charge any additional fees or credit any overpayment to Deposit Account 03-0935. Two additional copies of this letter are enclosed.

Respectfully submitted,

Kevin B. Clarke, Esq.
Attorney for Applicant
Registration No. 22,647
(212) 339-5207
Carter-Wallace, Inc.
1345 Avenue of the Americas
New York, New York 10105

Date: 12-18-96

CERTIFICATE OF MAILING

I hereby certify that this paper and the papers transmitted herewith are being deposited on the date shown below with the United States Postal Service with sufficient postage as First Class Mail addressed to Box Pat. Ext. Commissioner of Patents and Trademarks, Washington, DC 20231.

Date: 12-18-96

Kevin B. Clarke, Esq.
Name of Person Mailing Paper

Signature of Person Mailing Paper

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Patent of:	Helmut Hettche
Patent Number:	U.S. 5,164,194
Issued:	November 17, 1992
FOR:	AZELASTINE CONTAINING MEDICAMENTS

Commissioner of Patents and Trademarks
Washington, DC 20231

POWER OF ATTORNEY

Dear Sir:

Asta Medica, AG (formerly known as Asta Pharma AG), located at Frankfurt AM Main, Germany represents that it is the assignee of the entire interest in and to Letters Patent of the United States No. 5,164,194, granted to Helmut Hettche by virtue of an assignment of such patent recorded December 26, 1989, Reel 5237, Frame 0353 and hereby appoints

Kevin B. Clarke, Esq.
Reg. No. 22,647
C/O Carter-Wallace, Inc.
1345 Avenue of the Americas
New York, NY, U.S.A. 10105

its attorney, to apply for an extension of the term of said patent, to make alternations and amendments therein, and transact all business in the United States Patent Office connected therewith, and request that all further correspondence be conducted with Kevin B. Clarke at the above address.

Respectfully submitted,

By: _____
Dr. Klaus Rutz
Title: V.P. Business development
Date: Dec. 12. 1996

Asta Medica AG
By: _____
Professor Juergen Engel
Title: _____
Date: _____

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Patent of:	Helmut Hettche
Patent Number:	U.S. 5,164,194
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FOR:	AZELASTINE CONTAINING MEDICAMENTS

Box Pat. Ext.
Commissioner of Patents and Trademarks
Washington, DC 20231

DECLARATION IN SUPPORT OF APPLICATION
FOR PATENT EXTENSION UNDER 37 C.F.R. 1.740(b)

Dear Sir:

We, Dr. Klaus Rutz and Professor Juergen Engel, agents of the owner of record, Asta Medica, AG (formerly known as Asta Pharma, AG), of U.S. Patent No. 5,164,194 residing at Frankfurt AM Main Germany hereby declare as follows:

(1) This declaration is submitted in support of owner's Application for Extension of Patent Term for U.S. Patent No. 5,164,194, filed simultaneously herewith.

(2) We are officials of the owner of record of U.S. Patent 5,164,194 and are authorized to act on behalf of said owner.

(3) Wallace Laboratories, Division of Carter-Wallace, Inc., the holder of approved NDA No. 20-114 covering Wallace Laboratories azelastine hydrochloride product known as Astelin®, is a Licensee of owner under U.S. Patent 5,164,194.

(4) We have reviewed and understand the contents of the owner's Application for Extension of Patent term for U.S. Patent 5,164,194 being submitted herewith pursuant to 37 C.F.R. 1.740.

(5) We believe that U.S. Patent 5,164,194 is subject to extension pursuant to 37 C.F.R. 1.740 and believe that an extension of the length claimed in the Application for Extension of Patent Term for U.S. Patent 5,164,194 filed simultaneously herewith is justified under 35 U.S.C. 156 and the applicable requirements.

(6) We believe that U.S. Patent 5,164,194 for which extension is being sought meets the conditions for extension of the term of a patent as set forth in 37 C.F.R. 1.720.

We further state that the above statements were made with the knowledge that willful false statements and the like are punishable by fine or imprisonment or both under Section 1001 of Title 18 of the United States Code and that any willful false statements may jeopardize the validity of U.S. Patent No. 5,164,194.

By: _____
Dr. Klaus Rutz
Title: V.P. Business Development
Date: Dec. 12. 1996

Asta Medica AG
By: _____
Professor Juergen Engel
Title: _____
Date: _____

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE EXTENDING PATENT TERM
UNDER 35 U.S.C. § 156

PATENT NO.	:	5,164,194
ISSUED	:	November 17, 1992
INVENTOR(S)	:	Helmut Hettche
PATENT OWNER	:	Asta Medica, AG

This is to certify that there has been presented to the

COMMISSIONER OF PATENTS AND TRADEMARKS

an application under 35 U.S.C. § 156 for an extension of the patent term. Since it appears that the requirements of the law have been met, this certificate extends the term of the patent for the period of

349 days

from November 17, 2009, the original expiration date of the patent, subject to the payment of maintenance fees as provided by law, with all rights pertaining thereto as provided by 35 U.S.C. § 156(b).

I have caused the seal of the Patent and Trademark Office to be affixed this 27th day of February 1998.

Bruce A. Lehman

Bruce A. Lehman
Assistant Secretary of Commerce and
Commissioner of Patents and

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Patent of:	Helmut Hettche
Patent Number:	U.S. 5,164,194
Issued:	November 17, 1992
Expires:	November 17, 2009
FOR:	AZELASTINE CONTAINING MEDICAMENTS

Box Pat. Ext.
Commissioner of Patents and Trademarks
Washington, DC 20231

APPLICATION FOR EXTENSION OF PATENT TERM
UNDER 35 U.S.C. 156

Dear Sir:

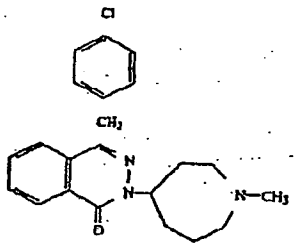
Applicant, Asta Medica, AG (formerly known as Asta Pharma, AG), represents that by virtue of an assignment recorded on December 26, 1989, at Reel 5237, Frame 0353, it is the assignee of the entire interest in and to Letters Patent of the United States No. 5,164,194 granted to Helmut Hettche. The claims of U.S. Patent No. 5,164,194 cover methods for using azelastine hydrochloride.

Pursuant to a license agreement dated August 16, 1982, Applicant granted Carter-Wallace, Inc., through its Wallace Laboratories Division, the exclusive right, with the right to grant sublicenses, to make, have made, use and sell the product azelastine in the United States of America together with the right to apply for, obtain and/or maintain investigational new drug exemptions ("IND's"), new drug applications ("NDA's") or other government clearances or approvals to market azelastine.

Azelastine hydrochloride NDA No. 20-114 which covers methods of using Wallace Laboratories' azelastine hydrochloride known as Astelin (hereafter the Approved Product) was approved on November 1, 1996.

Applicant hereby submits this application for extension of patent term under 35 U.S.C. 156, providing the following information as required by 37 C.F.R. 1.740:

(1) The Approved Product has the following structure:



(2) The Approved Product was subject to regulatory review under the Federal Food, Drug and Cosmetic Act (21 U.S.C. 355), Section 505.

(3) Applicant's licensee received permission for the commercial marketing or use of the Approved Product under Section 505 of the Federal Food, Drug and Cosmetic Act (21 U.S.C. 355) on November 1, 1996.

(4) This application for extension of patent term of United States Patent No. 5,164,194 under 35 U.S.C. 156 is being submitted within the sixty (60) day period permitted for submission, the last day for said submission being December 30, 1996.

(5) The complete identification of the patent for which an extension is being sought is as follows:

Inventor:	Helmut Hettche
Patent No.:	U.S. 5,164,194
Issued:	November 17, 1992
Expiration Date:	November 17, 2009

(6) A copy of the patent for which an extension is being sought is attached herewith as "Attachment A."

(7) A copy of the receipt for payment of the 4 year maintenance fee is attached herewith as "Attachment B."

(8) No disclaimer, certificate of correction, re-examination certificate or other receipt of maintenance fee payment has been issued with respect to U.S. Patent No. 5,164,194.

(9) U.S. Patent No. 5,164,194 claims methods for using the Approved Product, as identified in paragraph (1) hereinabove. More specifically, the methods are claimed in claims 1-9 and 12 of U.S. Patent No. 5,164,194 as follows:

(1) A method for the treatment of irritation or disorders of the nose and eye which comprises applying directly to nasal tissues or to the conjunctival sac of the eyes a medicament which contains a member selected from the group consisting of azelastine and its physiologically acceptable salts.

(2) A method as set forth in claim 1 in which the medicament contains 0.0005 to 2% (weight/weight) of azelastine or an amount of a physiologically acceptable salt of azelastine which contains 0.0005 to 2% (weight/weight) azelastine.

(3) A method as set forth in claim 2 in which the medicament contains 0.001 to 1% (weight/weight) of azelastine or an amount of a physiologically acceptable salt of azelastine which contains 0.001 to 1% (weight/weight) azelastine.

(4) A method as set forth in claim 1 in which the medicament contains 0.003 to 0.5% (weight/weight) of azelastine or an amount of a physiologically acceptable salt of azelastine which contains 0.003 to 0.5% (weight/weight) azelastine.

(5) A method as set forth in claim 1 in which the medicament contains a pharmaceutically usable preservative in an amount of 0.001 to 0.1%.

(6) A method as set forth in claim 1 in which the medicament is a solution.

(7) A method as set forth in claim 1 in which the medicament is an aqueous solution.

(8) A method as set forth in claim 1 in which the medicament is a solution which contains 0.001 to 0.05% (weight/volume of solution) of sodium-2-(ethylmercurithio)-benzoate or 0.001 to 0.1% (weight/volume of solution) of alkylbenzyldimethyl ammonium chloride.

(9) A method as set forth in claim 1 in which the medicament is applied by spraying.

(12) A method for the treatment of a patient suffering from allergy-related, or vasomotor or rhino-related colds or symptoms which comprises applying directly to the patient's nasal tissues or to the conjunctival sac of the patient's eye a medicament which contains a member selected from the group consisting of azelastine and its physiologically acceptable salts.

(10) The relevant dates and information pursuant to 35 U.S.C. 156(g) to enable the Secretary of Health and Human Services to determine the length of the applicable regulatory review period are as follows:

(a) U.S. Patent No. 5,164,194 was issued on November 17, 1992. U.S. Patent No. 5,164,194 is set to expire on November 17, 2009;

(b) IND for the Approved Product was filed by Wallace Laboratories on January 31, 1989, received and accorded IND No. 32,704 on February 6, 1989 and was effective on February 6, 1989;

(c) NDA for the Approved Product was submitted by Wallace Laboratories on March 26, 1991 (NDA No. 20-114); and

(d) NDA No. 20-114 for the Approved Product was approved on November 1, 1996.

(11) A brief description of the activities undertaken by the Applicant's licensee during the applicable regulatory review period with respect to the Approved Product and the significant dates applicable to such activities is attached herewith as "Attachment C."

(12) Applicant is of the opinion that U.S. Patent No. 5,164,194 is eligible for extension under 35 U.S.C. 156 because it satisfies the requirements for such extension as follows:

(a) 35 U.S.C. 156(a)
U.S. Patent No. 5,164,194 claims the method of using the Approved Product;

(b) 35 U.S.C. 156(a)(1)
The term of U.S. Patent No. 5,164,194 has not expired before submission of this application for extension;

(c) 35 U.S.C. 156(a)(2)
The term of U.S. Patent No. 5,164,194 has never been extended;

(d) 35 U.S.C. 156(a)(3)
The application for extension is submitted by the agent of the owner of record of U.S. Patent No. 5,164,194 in accordance with the requirements of 35 U.S.C. 156(d) and the guidelines of the U.S. Patent and Trademark Office;

(e) 35 U.S.C. 156(a)(4)
The Approved Product has been subject to regulatory review period before its commercial marketing or use;

(f) 35 U.S.C. 156(a)(5)(A)
The permission for the commercial marketing or use of the Approved Product, after the regulatory review period is the first permitted commercial marketing or use of the product, under the provisions of the Federal Food, Drug and Cosmetic Act (21 U.S.C. 355) under which such regulatory review period occurred; and

(g) 35 U.S.C. 156(c)(4)
No other patent has been extended for the same regulatory review period for the Approved Product.

(13) The length of extension of the term of United States Patent No. 5,164,194 claimed by applicant is 349 days. The maximum allowable under 35 U.S.C. 156 (c)(3) since the addition of 349 days to the patent term would yield a patent term of 14 years from the date of approval of the Approved Product. The regulatory review period exceeds 349 days as shown by the following:

(a) The regulatory review period under 35 U.S.C. 156 (g)(1)(B)(i) and (ii) was from February 6, 1989 until November 1, 1996;

(b) United States Patent No. 5,164,194 issued on November 17, 1992, which was 1,380 days after commencement of the regulatory review period;

(c) The period of review "Testing Period" under 35 U.S.C. 156 (g)(1)(B)(i) was from February 6, 1989, until March 26, 1991, which is 779 days subject to the following limitation:

(1) deduction of 779 days which occurred on or before the issuance of United States Patent No. 5,164,194. Accordingly, zero days of regulatory review occurred during the "Testing Period".

(d) The period of review "Application Period" under 35 U.S.C. 156 (g)(1)(B)(ii) was from March 26, 1991, until November 1, 1996, which is 2046 days subject to the following limitation:

(1) deduction of 601 days which occurred on or before the issuance of United States Patent No. 5,164,194. Accordingly, 1445 days of regulatory review occurred during the Application Period.

(e) In the absence of the 14 year limitation imposed by 35 U.S.C. 156 (c)(3), noted above, the permissible period of extension of term of United States Patent No. 5,164,194 would have been 1445 days;

(f) In compliance with 35 U.S.C. 156 (c)(3) the period remaining on the term of United States Patent No. 5,164,194 after approval of the Approved Product 4748 days which when added to the 349 day extension claimed by applicant 5097 days is not in excess of 14 years and will give United States Patent No. 5,164,194 an expiration date of November 1, 2010.

(14) Applicant acknowledges a duty to disclose to the Commissioner of Patents and Trademarks and the Secretary of Health and Human Services any information which is material to any determination to be made relative to this application for extension.

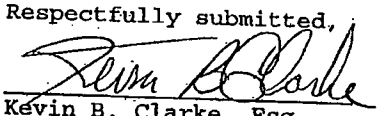
(15) The prescribed fee of $1090.00 for receiving and acting upon this application for extension is to be charged to Deposit Account 03-0935 as authorized in the accompanying letter which is submitted in duplicate. The requisite Declaration, set forth in 37 C.F.R. 1.740(a)(17) and (b) is also attached hereto.

(16) Inquiries and/or other correspondence relating to this application for patent term extension are to be directed to:

Kevin B. Clarke, Esq.
Carter-Wallace, Inc.
1345 Avenue of the Americas
New York, New York 10105

(17) A certified duplicate copy of the application papers is submitted herewith.

Respectfully submitted,



Kevin B. Clarke, Esq.
Attorney for Applicant
Registration No. 22,647
Carter-Wallace, Inc.
1345 Avenue of the Americas
New York, New York 10105
(212) 339-5207

TO WHOM IT MAY CONCERN:

CERTIFICATE

I hereby certify that the attached Application for Extension of Term of U.S. Patent 5,164,194 together with attachments thereto, Declaration in Support of Application for Patent Extension and Power of Attorney are true and duplicate copies of the originals of said documents filed with the United States Patent Office on this date.

Kevin B. Clarke, Esq.

date: 12-18-96

UNITED STAT EPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D. C. 20231

Attachment "B"

75M7/0509

CUSHMAN, DARBY & CUSHMAN
1100 NEW YORK AVENUE, N.W.
NINTH FLOOR
WASHINGTON, DC 20005-3918

MAINTENANCE FEE STATEMENT

The data shown below is from the records of the Patent and Trademark Office. If the maintenance fees and any necessary surcharges have been timely paid for the patents listed below, the notation "PAID" will appear in column 10, "status" below.

If a maintenance fee payment is defective, the reason is indicated by code in column 10, "status" below. An explanation of the codes appears on the reverse of the Maintenance Fee Statement. TIMELY CORRECTION IS REQUIRED IN ORDER TO AVOID EXPIRATION OF THE PATENT. NOTE 37 CFR 1.377. THE PAYMENT(S) WILL BE ENTERED UPON RECEIPT OF ACCEPTABLE CORRECTION. IF PAYMENT OR CORRECTION IS SUBMITTED DURING THE GRACE PERIOD, A SURCHARGE IS ALSO REQUIRED. NOTE 37 CFR 1.20(k) and (l).

If the statement of small entity status is defective the reason is indicated below in column 10 for the related patent number. THE STATEMENT OF SMALL ENTITY STATUS WILL BE ENTERED UPON RECEIPT OF ACCEPTABLE CORRECTION.

ITM NBR	PATENT NUMBER	FEE CDE	FEE AMOUNT	SUR CHARGE	SERIAL NUMBER	PATENT DATE	FILE DATE	PAY YR	SML ENT	STA
1	5,164,194	183	990	----	07/551,644	11/17/92	07/12/90	04	NO	PAID

If the "status" column for a patent number listed above does not indicate "PAID" a code or an asterisk (*) will appear in the "status" column. Where an asterisk (*) appears, the codes are set out below by the related item number. An explanation of the codes indicated in the "status" column and as set out below

** GESAMTSEITEN 002 **

ATTACHMENT "C"

Dates and brief descriptions of activities undertaken by Wallace Laboratories during the applicable regulatory review period for azelastine hydrochloride.

IND 32,704

January 31, 1989	IND for azelastine hydrochloride solution for intranasal use mailed to FDA by Wallace Laboratories.
February 6, 1989	IND received by FDA and assigned IND No. 32,704.
March 20, 1989	Wallace Laboratories letter responds to FDA telephone request for information concerning intranasal toxicity study in the rat.
May 22, 1989	FDA request for information concerning chemistry, manufacturing and control subjects and animal toxicology issues.
July 24, 1989	Wallace Laboratories submission in response to FDA request for information dated May 22, 1989.
August 4, 1989	Wallace Laboratories submission providing corrections to data submitted on March 20, 1989.
August 16, 1989	Clinical protocol 258 to assess safety, efficacy and duration of effect of several dosages of azelastine nasal spray and clinical investigator documentation submitted by Wallace Laboratories.
September 14, 1989	Clinical protocol 258 amendment to include additional investigator submitted by Wallace Laboratories.
November 22, 1989	Wallace Laboratories letter requesting a pre-NDA meeting.
December 21, 1989	Clinical protocol 272 to assess safety and efficacy of azelastine nasal spray and clinical investigator documentation submitted by Wallace Laboratories.
January 22, 1990	Wallace Laboratories submitted an updated Investigational Drug Brochure.
January 25, 1990	Wallace Laboratories acknowledged scheduling of a pre-NDA meeting and submitted information addressing format and content of integrated efficacy and safety data, individual clinical study information, case report tabulations, statistical analyses and foreign clinical experience.

IND 32,704

January 25, 1990	Wallace Laboratories submitted initial safety report from ongoing clinical trial.
January 30, 1990	Wallace Laboratories submitted updated pharmacology, toxicology and drug disposition information.
February 12, 1990	Clinical protocol 275 to assess safety and tolerability during extended treatment and clinical investigator documentation submitted by Wallace Laboratories.
February 13, 1990	Wallace Laboratories submitted new pharmacology information.
February 23, 1990	Annual report submitted by Wallace Laboratories.
February 26, 1990	Pre-NDA meeting convened with FDA.
March 6, 1990	Follow-up safety report submitted by Wallace Laboratories.
March 9, 1990	Wallace Laboratories submitted minutes from pre-NDA meeting.
April 9, 1990	Clinical protocol 281 to assess safety and efficacy and clinical investigator documentation submitted by Wallace Laboratories.
April 11, 1990	Clinical protocol 282 to assess safety and efficacy and clinical investigator documentation submitted by Wallace Laboratories.
April 12, 1990	Clinical protocol 272 amendment to define criteria for evaluating patient noncompliance submitted by Wallace Laboratories.
April 19, 1990	Clinical protocol 281 amendment to optimize patient compliance, data entry and data handling submitted by Wallace Laboratories.
May 4, 1990	Clinical protocol 283 to assess safety and efficacy and clinical investigator documentation submitted by Wallace Laboratories.
May 18, 1990	Clinical protocol 281 amendment to include additional investigator submitted by Wallace Laboratories.

azcchron

IND 32,704

May 25, 1990	Administrative notification of new location and phone numbers for medical monitors overseeing clinical development program.
July 7, 1990	Wallace Laboratories submitted initial safety reports from ongoing clinical trials.
September 20, 1990	Follow-up safety report submitted by Wallace Laboratories.
October 23, 1990	Wallace Laboratories submitted updated chemistry, manufacturing and control information.
January 9, 1991	Wallace Laboratories letter in preparation for FDA meeting to discuss environmental assessment issues for NDA.
January 16, 1991	Meeting with FDA to discuss environmental assessment issues for NDA.
February 14, 1991	Wallace Laboratories letter submitting minutes from the January 16, 1991 meeting concerning NDA environmental assessment issues.
March 15, 1991	Annual report submitted by Wallace Laboratories.
March 27, 1992	Annual report submitted by Wallace Laboratories.
August 13, 1992	Clinical protocol 315 to assess safety and efficacy as adjunctive therapy and clinical investigator documentation submitted by Wallace Laboratories.
August 26, 1992	Wallace Laboratories submitted updated chemistry, manufacturing and control information.
September 9, 1992	Clinical protocol 315 amendment concerning clinical investigator submitted by Wallace Laboratories.
March 8, 1993	Annual report submitted by Wallace Laboratories.
May 10, 1993	Clinical protocol 312 to assess safety and efficacy as adjunctive therapy and clinical investigator documentation submitted by Wallace Laboratories.

IND 32,704

June 4, 1993	Clinical protocol 312 amendment to include additional investigator submitted by Wallace Laboratories.
August 18, 1993	Clinical protocol 316 to assess safety and efficacy against beclomethasone and clinical investigator documentation submitted by Wallace Laboratories.
August 23, 1993	Wallace Laboratories letter requesting meeting with FDA to discuss adjunctive therapy clinical trials.
September 1, 1993	Clinical protocol 316 amendment addressing chemistry, manufacturing and control submitted by Wallace Laboratories.
September 9, 1993	Clinical protocol 316 amendment to include additional investigators submitted by Wallace Laboratories.
September 27, 1993	Clinical protocol 316 amendment to revise clinical investigator information submitted by Wallace Laboratories.
March 22, 1994	Annual report submitted by Wallace Laboratories.
February 24, 1995	Annual report submitted by Wallace Laboratories.
September 21, 1995	Wallace Laboratories submitted initial safety report from foreign source.
October 19, 1995	Follow-up safety report submitted by Wallace Laboratories.
November 30, 1995	Wallace Laboratories submitted initial safety report from foreign source.
December 1, 1995	Wallace Laboratories submitted initial safety report from foreign source.
January 19, 1996	Follow-up safety report submitted by Wallace Laboratories.
February 16, 1996	Annual report submitted by Wallace Laboratories.
March 22, 1996	Clinical protocol 362 to assess product acceptance by patients submitted by Wallace Laboratories.
May 2, 1996	Wallace Laboratories submitted initial safety report from foreign source.